

**II. REMARKS**

Applicant amends claims 27, 29, 32 and 34-39 to correct typographical errors and provide proper antecedent basis for the claims. No new matter has been added.

## AMENDMENTS TO THE CLAIMS

1. (Previously Presented) An isolated antibody or antibody fragment thereof which comprises an antigen-binding domain of a human antibody specific for human TGF $\beta$ .
2. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 which is in the form of scFv.
3. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 which is in the form of a whole antibody.
4. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises part or all of a VH domain encoded by a germ line gene segment or a rearranged gene segment.
5. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises part or all of either a VL kappa domain or a VL lambda domain.
6. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VH domain consisting of the amino acid sequence as shown in any one of Fig. 1(a)(i) to (iv) (SEQ ID NOS: 8, 111, 112 and 10) or Fig. 1(c)(i) (SEQ ID NO: 12).
7. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain consisting of the amino acid

sequence as shown in any one of Fig. 1(a)(v) (SEQ ID NO: 14) or Fig. 1(b) (SEQ ID NOS: 16 and 18).

8. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VH domain consisting of the amino acid sequence as shown in any one of Fig. 2(a)(i) to (iii) (SEQ ID NOS: 6, 37 and 116), (v) (SEQ ID NO: 120), and (vi) (SEQ ID NO: 122).

9. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain consisting of the amino acid sequence as shown in any one of Fig. 2(a)(iv) (SEQ ID NO: 118) or Fig. 2(b)(i) to (vi) (SEQ ID NOS: 39, 41, 43, 45, 47, 124).

10. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain consisting of the amino acid sequence as shown in Fig. 4 (SEQ ID NO: 49).

11. (Previously Presented) An antibody or antibody fragment thereof according to claim 1 wherein the antigen-binding domain comprises a VL domain encoded by the nucleotide sequence as shown in Fig. 4 (SEQ ID NO: 48).

12. (Previously Presented) A polypeptide with a binding domain specific for TGF $\beta$  which polypeptide comprises an amino acid sequence as shown in any one of Fig. 1(a) (SEQ ID NOS: 8, 111, 112, 10, 14), Fig. 1(b) (SEQ ID NOS: 16 and 18), Fig. 1(c) (SEQ ID NO: 12), Fig. 2(a)

(SEQ ID NOS: 6, 37, 116, 118, 120 and 122), Fig. 2(b) (SEQ ID NOS: 39, 41, 43, 45, 47, 124), and Fig. 4 (SEQ ID NO: 49).

**13.** (Previously Presented) An isolated antibody or antibody fragment thereof comprising an antigen-binding domain of a human antibody specific for human TGF- $\beta$ , said antigen-binding domain comprising the VH domain 6H1 VH of which the amino acid sequence is shown in Figure 2(a)(i) (SEQ ID NO: 6).

**14.** (Previously Presented) An antibody or antibody fragment thereof according to claim 13 which is in the form of scFv.

**15.** (Previously Presented) An antibody or antibody fragment thereof according to claim 13 which is in the form of a whole antibody.

**16.** (Previously Presented) An antibody or antibody fragment thereof according to claim 13 wherein said antigen-binding domain of a human antibody comprises a VL domain selected from 6B1 VL, of which the amino acid sequence is shown in Figure 2(b)(iii) (SEQ ID NO: 43), 6H1 VL, of which the amino acid sequence is shown in Figure 2(b) (vi) (SEQ ID NO: 124), and 6A5 VL, of which the amino acid sequence is shown in Figure 2(b)(ii) (SEQ ID NO: 41).

**17.** (Previously Presented) An antibody or antibody fragment thereof according to claim 16 which is in the form of scFv.

**18.** (Previously Presented) An antibody or antibody fragment thereof according to claim 16 which is in the form of a whole antibody.

**19.** (Previously Presented) An isolated antibody or antibody fragment thereof comprising an antigen-binding domain of a human antibody specific for human TGF $\beta$ , said antigen-binding domain of a human antibody comprising the VH domain 6H1 VH of which the amino acid sequence is shown in Figure 2(a)(i) (SEQ ID NO: 6) and the VL domain 6B1 VL, of which the amino acid sequence is shown in Figure 2(b)(iii) (SEQ ID NO: 43).

**20.** (Previously Presented) An antibody or antibody fragment thereof according to claim 19 which is in the form of scFv.

**21.** (Previously Presented) An antibody or antibody fragment thereof according to claim 19 which is in the form of a whole antibody.

**22.** (Previously Presented) A composition which comprises an antibody or antibody fragment thereof, according to claim 13 and an excipient.

**23.** (Previously Presented) A composition which comprises an antibody or antibody fragment thereof, according to claim 19 and an excipient.

**24.** (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said human antibody antigen binding domain comprises a VH domain which has the amino acid sequence shown in Figure 1 (a) (i) (SEQ ID NO: 8).

**25.** (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially

over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said human antigen binding domain comprises a VL domain which has the amino acid sequence shown in Figure 14 (SEQ ID NO: 59).

**26.** (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said human antibody antigen binding domain comprises a pairing of a VH domain and a VL domain selected from:

- (a) 1B2 VH, of which the amino acid sequence is shown in Figure 1 (a) (i) (SEQ ID NO: 8), and 7A3 VL, of which the amino acid sequence is shown in Figure 1 (b) (i) (SEQ ID NO: 16);
- (b) 31G9 VH, of which the amino acid sequence is shown in Figure 1 (a) (iv) (SEQ ID NO: 10), and 31G9 VL, of which the amino acid sequence is shown in Figure 1 (a) (v) (SEQ ID NO: 14); and
- (c) 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ ID NO: 12), and 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

**27.** (Currently Amended) A specific binding member according to claim [[18]] **26** wherein said human antibody antigen binding domain comprises a VH domain 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ ID NO: 12), and the VL domain 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

**28.** (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said human antibody antigen binding domain comprises a VH domain which comprises a CDR3 with an amino acid sequence selected from those shown in Figure 3 (SEQ ID NOS: 19-35).

**29.** (Currently Amended) A specific binding member according to claim ~~[[20]]~~ **28** wherein said CDR3 has the sequence shown for CDR3 of 27C1 VH (SEQ ID NO: 12). (BUT NO ANTECEDENT BASIS FOR SEQ ID NO:12)

**30.** (Previously Presented) A specific binding member comprising a human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said human antibody antigen binding domain comprises the 31 G9 VH domain of which the amino acid sequences is shown in Figure 1 (a) (iv) (SEQ ID NO: 10) and the CS37 VL of which the sequence is shown in Figure 14 (SEQ ID NO: 59).

**31.** (Previously Presented) A specific binding member which is a first specific binding member comprising a first human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said first specific binding member competes for binding to TGF $\beta$ 1 with a second specific binding member comprising a second human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, wherein said second human antibody antigen binding domain comprises a pairing of a VH domain and a VL domain selected from:

- (a) 1 B2 VH, of which the amino acid sequence is shown in Figure 1 (a) (i) (SEQ ID NO: 8), and 7A3 VL, of which the amino acid sequence is shown in Figure 1 (b) (i) (SEQ ID NO: 16);
- (b) 31G9 VH, of which the amino acid sequence is shown in Figure 1(a) (iv) (SEQ ID NO: 10), and 31G9 VL, of which the amino acid sequence is shown in Figure 1 (a) (v) (SEQ ID NO: 14); and
- (c) 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ

ID NO: 12), and the VL domain 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).

- 32.** (Currently amended) A first specific binding member according to claim ~~[[23]]~~ **31**, wherein said second human antibody antigen binding domain comprises the VH domain 27C1 VH, of which the amino acid sequence is shown in Figure 1 (c) (i) (SEQ ID NO: 12), and the VL domain 10A6 VL, of which the amino acid sequence is shown in Figure 1 (b) (ii) (SEQ ID NO: 18).
- 33.** (Previously Presented) A specific binding member which is a first specific binding member comprising a first human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, and wherein said first specific binding member competes for binding to TGF $\beta$ 1 with a second specific binding member comprising a second human antibody antigen binding domain specific for human TGF $\beta$  isoform TGF $\beta$ 1 which binds TGF $\beta$ 1 preferentially over TGF $\beta$ 3 and which neutralizes TGF $\beta$ 1, and wherein said second human antibody antigen binding domain comprises the 31 G9 VH domain of which the sequence is shown in Figure 1 (a) (iv) (SEQ ID NO: 10) and the CS37 VL of which the sequence is shown in Figure 14 (SEQ ID NO: 59).
- 34.** (Currently Amended) A specific binding member as in any one of claims ~~16, 17, 18, 20, 22, 23, or 25~~ **24, 25, 26, 28, 30, 31 or 33** comprising a single-chain Fv antibody molecule.
- 35.** (Currently Amended) A specific binding member as in any one of claims ~~16, 17, 18, 20, 22, 23, or 25~~ **24, 25, 26, 28, 30, 31 or 33** which comprises one or more amino acids in addition to those forming said human antibody antigen binding domain.



- 36.** (Currently Amended) A specific binding member according to claim ~~[[31]]~~ **35** comprising an antibody constant region.
- 37.** (Currently Amended) A specific binding member according to claim ~~[[32]]~~ **36** which comprises a whole antibody.
- 38.** (Currently Amended) A specific binding member according to claim ~~[[32]]~~ **36** wherein said antibody constant region is IgG4 isotype.
- 39.** (Currently Amended) A pharmaceutical composition comprising a specific binding member as in any one of claims ~~16, 17, 18, 20, 22, 23, or 25~~ **24, 25, 26, 28, 30, 31 or 33** and a pharmaceutically acceptable excipient.

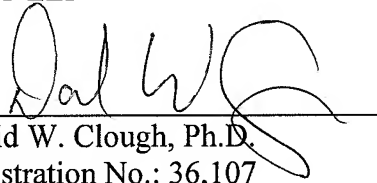
**CONCLUSION**

The Examiner is hereby respectfully invited to contact the undersigned attorney at the number listed below with any questions, comments or suggestions relating to this application.

Respectfully submitted,

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